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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte YASMIN THANAVALA

Appeal 2008-4835
Application 09/464,414
Technology Center 1600

Decided: January 12, 2009

Before DONALD E. ADAMS, ERIC GRIMES, and MELANIE L. McCOLLUM, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to providing a secondary boosting immune response. The Examiner has rejected the claims as nonenabled. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

"Pathogenic microorganisms . . . that do not raise a protective enteric immune response in mammals" are referred to as non-enteric pathogens (Spec. 1). "'Non-enteric pathogen antigen' (NEPA) means an antigen that will parenterally raise an immune response to a non-enteric pathogen" (*id.* at 5).

Claims 1-3, 7, 9, 10, and 13 are pending and on appeal. We will focus on claim 1, the broadest claim on appeal, which reads as follows:

> 1. A method for providing a secondary boosting immune response in a mammal to a specific antigen of a non-enteric pathogen (NEPA), the pathogen being a pathogen that invades through a breach in the skin and that does not itself enterically raise a primary protective immune response in mammals in the absence of prior acquired immunity to the pathogen, said method comprising:
>
> rendering the mammal immunoreceptive to the NEPA by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection; and
>
> then orally administering the NEPA to the immunoreceptive mammal by feeding the mammal with transgenic potato containing the NEPA expressed in the potato to enterically cause a secondary immune response to the oral administration specific to the NEPA stronger than would be caused by orally administering the NEPA in the absence of the prior immunization by injection.

Claims 1-3, 7, 9, 10, and 13 stand rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling . . . wherein the NEPA is hepatitis B surface antigen (HBsAg) . . . , does not reasonably provide enablement for providing a secondary boosting immune response in a mammal to any and all NEPAs" (Ans. 4). In particular, the Examiner finds:

> The specification broadly discloses non-enteric pathogens that invade the epidermis of mammals via punctures, abrasions, cuts or other breaches in the skin, *e.g.*, blood transfusions which can be used as sources of NEPA to raise a protective enteric immune response in mammals. However, the specification does not provide sufficient guidance as to how one of ordinary skill in the art would provide an immune response in a mammal and/or a human to a NEPA other than the non-enteric pathogen antigen, hepatitis B surface antigen.

(*Id.* at 5.)

The Examiner "concedes that one skilled in the art at the time the invention was made would have known how to make and/or use a plant to express a viral immunogen (antigen) for the oral administration thereof to elicit an immunogenic response" (*id.* at 8). However, the Examiner finds that Appellant "has not provided sufficient guidance as to how one . . . would render a mammal immunoreceptive to an antigen of any and all non-enteric pathogens" (*id.* at 9).

In particular, the Examiner finds that "the art[s] of virology, microbiology, and immunology are highly unpredictable" (*id.* at 10). The Examiner also finds that "effective immunization treatments for providing immunological responses in mammals, much less humans, to the disclosed non-enteric pathogens are moderately rare, controvertible, and in some instances unsafe; and, therefore, may be unbelievable in the absence of supporting evidence" (*id.* at 10-11). In addition, the Examiner finds that "the state of the art at the time of filing suggests that the functional effect for rendering a mammal immunoreceptive to any and all NEPAs by prior immunization via vaccination by injection . . . was atypical or not available" (*id.* at 11).

As evidence that the claims are nonenabled, the Examiner refers to the following references:

Simona Bratu & Larry I. Lutwick, *Active immunisation against human tick-borne diseases*, 2 EXPERT. OPIN. BIOL. THER. 187-195 (2002) (hereinafter "Bratu");

Richard W. Titball & E. Diane Williamson, *Vaccination against bubonic and pneumonic plague*, 19 VACCINE 4175-4184 (2001) (hereinafter "Titball");

John R. Stephenson, *Genetically Modified Viruses: Vaccines by Design*, 2 CURRENT PHARMACEUTICAL BIOTECHNOLOGY 47-76 (2001) (hereinafter "Stephenson"); and

Patrizia Farci et al., *Lack of Protective Immunity Against Reinfection with Hepatitis C Virus*, 258 SCIENCE 135-140 (1992) (hereinafter "Farci").

Appellant contends that it "is true that a number of diseases may not have vaccines with FDA or WHO approval, but it is not true that vaccines do not exist" (Reply Br. 1-2). Appellant notes that the issue of FDA or WHO approval "is not the same as whether vaccines can be made by those skilled in the art against the above diseases" (*id.* at 2).

ISSUE

Has the Examiner set forth a prima facie case that the Specification does not enable rendering a mammal immunoreceptive to the claimed NEPA by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection?

FINDINGS OF FACT

1. The Specification states that "[e]xamples of diseases caused by non-enteric pathogens are: hepatitis B, hepatitis C, hepatitis delta, yellow fever, Lassa fever, dengue hemoragic [sic] fever, rabies, tetanus,

staphylococcus aureous [sic] infections, yaws, relapsing fever, rat bite fever, bubonic plague, typhoid fever and spotted fever" (Spec. 1).

2. The Specification states that "an immune response to non-enteric pathogen antigens, e.g., hepatitis B surface antigen (HBsAg) may be obtained when the antigen in a plant material is fed to the animal when the animal is immunoreceptive to the HBsAg" (*id.* at 4).

3. The Specification also states that the animal may "be immunoreceptive due to a prior , e.g. primary, immunization" (*id.*).

4. In particular, the Specification states that "an animal, e.g. a human, that previously had a positive response to primary immunization against hepatitis B, can have a booster response to HBsAg by feeding the animal the antigen in a plant material" (*id.*).

5. The Specification also discloses that the primary immunization may be administered by "parental [sic, parenteral] injection" (*id.* at 6).

6. Bratu states that "[c]urrently there is no licensed vaccine available for protection against *R. rickettsii*," the causative organism for Rocky Mountain spotted fever (Bratu 191).

7. Bratu also states:

> A formalin-killed, purified *R. rickettsii* vaccine was developed from rickettsiae propagated in cell cultures. The vaccine induces production of serum antibodies as well as a variable degree of cell-mediated immune responses but studies in both animals and human volunteers showed that it provides only partial immunity with a vaccine efficacy reported of approximately 25%.

(*Id.*)

8. Titball states that "[b]oth live attenuated and killed whole cells vaccines have been used in man [against plague]. . . . Although there is circumstantial evidence for the efficacy of these vaccines, none have been subjected to a controlled and randomised clinical trial." (Titball 4177.)

9. In particular, Titball states that "immunisation with the EV76 [live attenuated] vaccine will provide protection against both bubonic and pneumonic plague in man. However, the safety of this vaccine in man is questionable, because the EV76 strain is not avirulent. In studies with mice, a fatality rate of approximately 1% of [vaccines] has been reported." (*Id.*) Titball also states that "in most countries [the live attenuated vaccine] is not considered to be suitable for use in humans" (*id.* at 4175).

10. In addition, Titball states that there "are no definitive clinical trials which demonstrate the efficacy of killed whole cell vaccines. . . . However, studies in several animal species have demonstrated protection against bubonic plague," although "findings suggest that killed whole cell vaccines do not induce a response which provides protection against pneumonic plague." (*Id.* at 4177.)

11. Stephenson states that "there is still no commercially available dengue vaccine" (Stephenson 49).

12. Stephenson also states that there is no commercially available vaccine for hepatitis C (*id.* at 49: Table 2).

13. In addition, Stephenson lists several diseases for which there is a commercially available vaccine. These diseases include hepatitis B, rabies, and yellow fever. (*Id.* at 48: Table 1.) Hepatitis B, rabies, and yellow fever are among the diseases listed in the Specification as

"[e]xamples of diseases caused by non-enteric pathogens" (Finding of Fact (FF) 1).

14. Farci states that "evidence indicates that HCV [hepatitis C virus] infection does not elicit protective immunity against reinfection with homologous or heterologous strains, which raises concerns for the development of effective vaccines against HCV" (Farci 135: Abstract).

PRINCIPLES OF LAW

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 439 F.2d 220, 223 (CCPA 1971). In addition, "a patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986).

"It is [also] well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art." *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991).

> Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. "It is not a function of the

> claims to specifically exclude . . . possible inoperative substances. . . ." *In re Dinh-Nguyen*, 492 F.2d 856, 858-59 . . . (CCPA 1974). . . . Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid.

Atlas Powder Co. v. E.I. du Pont De Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984) (citations omitted). "[S]ufficient disclosure . . . to teach those of ordinary skill how to make and how to use the invention . . . means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *Vaeck*, *supra*.

"[T]he PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application." *Wright*, 999 F.2d at 1561-62. "[T]his includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. If the PTO meets this burden, the burden then shifts to the applicant to provide suitable proofs indicating that the specification is indeed enabling." *Id.* at 1562.

ANALYSIS

The Examiner provides evidence that there are no commercially available vaccines for some of the diseases indicated in the Specification to be caused by non-enteric pathogens (FF 6, 9, 11, & 12). However, we agree with Appellant that evidence that commercially available vaccines are not available is not evidence that one of ordinary skill in the art would not have

known how to render mammals immunoreceptive to these NEPAs by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection (Reply Br. 1-2).

The Examiner also provides evidence indicating that, for one disease caused by a non-enteric pathogen, hepatitis C, the virus "does not elicit protective immunity against reinfection with homologous or heterologous strains, which raises concerns for the development of effective vaccines against HCV" (FF 14). However, evidence of a possible inoperative embodiment is not sufficient to render claim 1 nonenabled. "It is not a function of the *claims* to specifically exclude . . . possible inoperative substances." *In re Dinh-Nguyen*, 492 F.2d 856, 858-59 (CCPA 1974).

CONCLUSION

The Examiner has not set forth a prima facie case that the Specification does not enable rendering a mammal immunoreceptive to the claimed NEPA by prior immunization against a non-enteric pathogen containing the NEPA by vaccination by injection. We therefore reverse the enablement rejection of claim 1 and of claims 2, 3, 7, 9, 10, and 13, which depend from claim 1.

REVERSED

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